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Neuroinflammation and Alzheimer's Dementia

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Abstract

Amyloid beta clusters have been found to accumulate faster in the presence of cholesterol in brain cell membranes. L5, the most negatively charged LDL, is the most potent in inducing endothelial cell reactive oxygen species (ROS) and apoptosis. TNF-α and PGE2 levels significantly increased in the microglia treated with metVLDL, indicated through microglia activation and neuroinflammation. In C57BL/6 mice, repeated injections of metVLDL, containing more V5 elicited an early decline in cognitive functions. The AD patients with higher L5 % (L5>=1.5%) have worse baseline cognitive functions including MMSE and CASI and global severity of dementia (CDR-SB) as well as more rapid deterioration of cognition. Our findings highlighted the importance of the novel approach to Alzheimer's disease from electronegative lipoproteins.

The shift from normal glucose (NG; 5.5 mM) to high glucose (HG; 25 mM) promoted cell growth and induced oxidative/inflammatory stress and microglial activation, as evidenced by increased MTT reduction, elevated pro-inflammatory factor secretion, and upregulated expression of stress/inflammatory proteins, which led to apoptosis and autophagy. LPS-induced inflammation was enlarged by an NG-to-HG shift. Acute glucose fluctuation forms the stress that altered microglial activity, representing a novel pathogenic mechanism for the continued deterioration of neurological function in diabetic patients.

REST (RE1-silencing transcription factor) gene has been shown to be lost in Alzheimer's disease (AD). The allele frequency of rs3796529-T was significantly lower in the AD cohort compared to the general population cohort (36.82% vs. 40.73%, p=0.029). The AD patients carrying the rs3796529 T/T genotype had a longer progression-free survival than those with the C/C genotype (p=0.012). In multivariate analysis, the rs3796529 T/T genotype (adjusted HR=0.593, 95% CI: 0.401-0.877, p=0.009) was an independent protective factor for functional deterioration.

Our findings suggested that neuro-inflammation could be an important pathogenesis for AD and anti-inflammatory agents should also be considered in the therapy for AD.

Biography

Ching-Kuan Liu studied medicine at Kaohsiung Medical College, Taiwan and received M.D in 1982, residency in Neurology at KMU Hospital during 1982-1986, MS in 1986 and, Ph.D. in 1992 at KMU. He took the Clinical Instructor of Neurobehavior Program at UCLA from 1988 to 1990 and the fellowship of clinical Neurophysiology in 1989. In 2000, he was promoted to Professor of Neurology and became chairman of Neurology, dean of division of Info Tech from 2002 to 2006, the vice-superintendent of KMUH from 2006 to 2009, the Superintendent of KMHKH from 2009 to 2012. He has also elected as the president of Taiwan Dementia Society and Taiwan Neurology Society in 2006 and 2007 and being the Delegate of WFN of Taiwan from 2012 to 2015. He was the President of KMU from July 2012 to June 2018. His current areas of research are dementia, clinical neuropsychology, and behavioural neurology.

Publications

1. CAssociation of early-onset Alzheimer's disease with germline-generated high affinity self-antigen load
2. Acute glucose fluctuation impacts microglial activity, leading to inflammatory activation or self-degradation
3. ALVQ-Based Identification System for Pathological Brain Aging Diseases
4. Immunoregulatory effects of very low density lipoprotein from healthy individuals and metabolic syndrome patients on glial cells
5. Compensatory Neural Recruitment for Error-Related Cerebral Activity in Patients with Moderate-To-Severe Obstructive Sleep Apnea
6. A 48-Week, Multicenter, Open-Label, Observational Study Evaluating Oral Rivastigmine in Patients with Mild-to-Moderate Alzheimer's Disease in Taiwan
7. Association of Hyperglycemia Episodes on long-term mortality in type 2 diabetes mellitus with vascular dementia: A population-based cohort study

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